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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,137	01/19/2005	Kenichi Yamashita	2005_0047A	2521

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EXAMINER	
POHNERT, STEVEN C	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,137	YAMASHITA ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/27/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to papers filed 11/23/2007.

2. The papers filed have amended claims 1, 2 and 4 and canceled claim 3.

3. Claims 1 and 4 have been amended to require new limitations that have not been previously presented including: quantitative analysis, fluorescent probes and comparing to quantitatively analyze specimen molecules.

4. The 112-2nd paragraph rejection of claims 1,2, and 4 for lacking a positive active step referring back to the preamble has been overcome by amendment to claims 1 and 4.

5. The 112-2nd paragraph rejections of claims 1, 2, and 4 for lacking positive active steps has been overcome as the claims have been amended to passing a solution, promoting diffusion and determining degree of diffusion.

6. The 102 rejection of Garman has been overcome, as the claims now require a calibration curve, however, Garman does not teach a calibration curve.

7. This action is Final.

Claim Objections

8. Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 depends from claim 1 and recites in the second line, " wherein the fluorescent probe molecules are capable of emitting fluorescence." However, claim 1 recites "detecting signals emitted

from the fluorescent probe molecules." Thus as claim 1 requires fluorescent probe molecules by emitting a signal, claim 2 fails to further limit.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolinsky, et al (WO 1994/00598, published January 6, 1994).

With regards to claims 1, 2, and 4, Wolinsky et al teaches a method of analyzing a specimen by detection of DNA sequences by flow cytometry (see abstract). Wolinksy et al teaches a solution containing FITC-tagged oligonucleotide probes was added to samples in which PCR amplification had been done (see page 12, 1st paragraph). Wolinsky teaches the samples were allowed to hybridize (form a complex) and then analyzed by flow cytomtery (see page 12, 2nd paragraph). Flow cytometry is analysis of a sample in laminar flow through a microflow channel. Wolinsky et al further teaches detection of the complex by excitation of the fluorescent dyes (FITC and propidium iodine (PI)) (see page 13 1st paragraph). Wolinsky thus teaches a method of analyzing a DNA sample (specimen) by causing a solution containing the DNA and a solution containing fluorescent probe to promote diffusion by laminar flow and detect the presence of the specimen molecule by altered diffusion relative to the specimen molecule and probe molecules.

Wolinsky teaches the instrument was calibrated using calibration beads before each assay and a standard curve was produced (see page 13). Wolinsky et al thus analysis of the degree of diffusion was carried out in reference to a calibration curve.

Response to arguments

The response asserts that Wolinsky does not disclose the comparison of the results obtained to a pre-determined calibration curve. These arguments have been thoroughly reviewed but are not conisdered persuasive as Wolinsky demonstrates that the standard curve determined the sensitivity and specificity of the assay was99.6% and 99.2% (see page 13, last 2 lines of first paragraph). Thus Wolinsky anticipates each and every limitation of the claims.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 2 and 4 rejected under 35 U.S.C. 103(a) as being unpatentable over Wolinsky, et al (WO 1994/00598, published January 6, 1994) in view of Chee et al (US Patent 6355431, published March 12, 2002).

With regards to claims 1, 2, and 4, Wolinsky et al teaches a method of analyzing a specimen by detection of DNA sequences by flow cytometry (see abstract). Wolinksy et al teaches a solution containing FITC-tagged oligonucleotide probes was added to samples in which PCR amplification had been done (see page 12, 1st paragraph). Wolinsky teaches the samples were allowed to hybridize (form a complex) and then analyzed by flow cytomtery (see page 12, 2nd paragraph). Flow cytometry is analysis of a sample in laminar flow through a microflow channel. Wolinsky et al further teaches detection of the complex by excitation of the fluorescent dyes (FITC and propidium iodine (PI)) (see page 13 1st paragraph). Wolinsky teaches the instrument was calibrated using calibration beads before each assay and a standard curve was produced (see page 13). Wolinsky thus teaches a method of analyzing a DNA sample (specimen) by causing a solution containing the DNA and a solution containing fluorescent probe to promote diffusion by laminar flow and detect the presence of the specimen molecule by altered diffusion relative to the specimen molecule and probe molecules.

Wolinsky does not teach explicitly teach comparing the results of the assay to a calibration curve obtained by the use of immunobright clibration beads to quantitatively analyze the sample.

However, Chee et al teaches quantitation of nucleic acids based on the signals generated by the sample of interest that is then compared to a calibration curve to measure the concentration of the analyte (column 58, lines 25-40).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Wolinsky by combining it with the quanitation methods of Chee with a reasonable expectation of success as both Wolinksy and Chee are drawn to detecting nucleic acids. The skilled artisan would have been motivated to combine the teachings of Wolinsky and Chee because Chee teaches the comparison analyte data to calibration curves allows the artisan to determine the amount of analyte present. The combination Chee and Wolinksy would result in a method to quantitate the amount of a target analyte in a sample by use of a calibration curve.

Response to arguments

The response asserts that Wolinksy does not disclose or suggest promoting selective diffusion of the complex. This argument has been thoroughly reviewed but is not considered persuasive as the specification does not set forth a limiting definition of "selectively promoting diffusion." Thus the diffusion of the complex in the laminar flow relative to the free probe is interpreted as selectively promoting diffusion.

The response further asserts that Wolinsky does not teach fluorometrically determining the degree of diffusion of the complex. This argument has been thoroughly reviewed but is not considered persuasive because Wolinsky teaches fluorescent detection of the complex in the flow cytometric analysis (page 13), which is determining the degree of diffusion relative to the unbound probe fluorometrically.

New Grounds of Double Patenting Necessitated by Amendment

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1and 4 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims1 and 3 of copending Application No. 10/527,987 in further view of Chee et al (US Patent 6355431, published March 12, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are coextensive in scope. This is a

provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1 is drawn to a method for analyzing specimen molecules which comprises: a step to cause flowing of a solution containing the specimen molecules and a solution containing probe molecules capable of forming a complex with the specimen molecules in a micro flow channel in such a fashion that a laminar flow is formed; a step to selectively promote diffusion of the complex formed according to the affinity in the laminar flow, and a step to detect and analyze the degree of diffusion of the complex formed between the specimen molecules and the probe molecules.. Claim 1 of '987 teaches a carrying out a reaction by utilizing a micro flow channel characterized in that, in carrying out a chemical reaction of two kinds or more of reactants capable of reacting each with the others, molecules of the reactants as carried by a fluid are introduced into a micro flow channel and the chemical reaction is carried out efficiently by utilizing interactions of the micro flow channel to cause changes in the molecular structure, molecular orientation or distribution of the molecules in the solution. Claim 3 of '987 teaches laminar flow. Claim 1 of instant application is obvious over claims 1 and 3 of '987 as they both require the use of a micro flow channel and the two reactants. The two reactants of claims 1 and 3 of '987 are a specimen and probe, thus the claims are obvious.

Claim 4 of the instant application is drawn to a method for analysis of a DNA fragment which comprises: a step to cause flowing of a solution containing a DNA fragment of a specified sequence as a specimen molecule and a solution containing a

probe molecule capable of forming a complex with the specimen molecule in a micro flow channel in such a fashion that a laminar flow is formed; a step to selectively promote diffusion of the complex formed according to affinity in the laminar flow; and a step to detect and analyze the degree of diffusion of the complex formed between the specimen molecule and the probe molecule. Claim 1 of '987 teaches a carrying out a reaction by utilizing a micro flow channel characterized in that, in carrying out a chemical reaction of two kinds or more of reactants capable of reacting each with the others, molecules of the reactants as carried by a fluid are introduced into a micro flow channel and the chemical reaction is carried out efficiently by utilizing interactions of the micro flow channel to cause changes in the molecular structure, molecular orientation or distribution of the molecules in the solution. Claim 3 of '987 teaches laminar flow,. . Claim 4 of instant application is obvious over claim 1 and 3of '987 as they both require the use of a micro flow channel and the two reactants. The two reactants of claims 1 and 3 of '987 broadly encompass a DNA fragment and probe, thus the claims are obvious.

The claims of '987 do not teach comparing the results of the assay to a calibration curve to quantitatively analyze the sample.

However, Chee et al teaches quantitation of nucleic acids based on the signals generated by the sample of interest that is then compared to a calibration curve to measure the concentration of the analyte (column 58, lines 25-40).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of '987 by combining it

with the quanitation methods of Chee with a reasonable expectation of success. The skilled artisan would have been motivated to combine the teachings of '987 and Chee because Chee teaches the comparison analyte data to calibration curves allows the artisan to determine the amount of analyte present. The combination Chee and '987 would result in a method to quantitate the amount of a target analyte in a sample by use of a calibration curve.

Summary

No claims are allowed.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Ram R. Shukla/
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